EXPEDITED PROCEDURE – EXAMINING GROUP 1623

S/N 09/458,862 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Allison Hubel	Examiner: Elli Peselev
Serial No.:	09/458,862	Group Art Unit: 1623
Filed:	December 10, 1999	Docket: 600.451US1
Title:	COMPOSITIONS AND METHODS FOR CRYOPRESERVATON OF PERIPHERAL BLOOD LYMPHOCYTES	

DECLARATION UNDER 37 C.F.R. 1.132

Sir:

I, John C. Bischof, Ph.D., declare and say as follows:

1. I am a Professor in the Department of Mechanical Engineering at the University of Minnesota. I received a B.S. and a M.S. in Biomedical Engineering, followed by a Ph.D. in Mechanical Engineering. My research involves understanding the response of cells to changes in temperature. The majority of these studies have involved the study of cells at freezing temperatures. I have published 35 peer reviewed journal articles in the field of what is termed cryobiology and I am the president elect for the Society for Cryobiology.

2. I am familiar with the specification for the above-identified application and WO 97/35472, and I make this Declaration in support of the patentability of the claims of the above-identified application.

3. Prior to the filing of the above-identified application, there was still a considerable need for the development and refinement of cryopreservation solutions and protocols. In particular, solutions and protocols developed for cells which were amenable to cryopreservation and employable in cellular-based therapies, frequently resulted in suboptimal levels of post thaw viability and, more often than not, employed protective agents that were harmful upon infusion.

4. It is a frequent misconception that a universal solution or protocol for preservation of mammalian cells can be developed. The fundamental physical phenomena present during freezing are strongly influenced by the composition of the freezing solution and the cell type being preserved. Thus, protocols and solutions developed for one cell type may not be appropriate for another. Accordingly, the broad, general disclosure in WO 97/35472 related to protocols and arabinogalactan containing solutions for the cryopreservation of a variety of cells is not supported by the scientific knowledge in the field, i.e., based on the data in WO 97/35472 one skilled in the relevant field would not have a reasonable expectation that the protocols and solutions disclosed in WO 97/35472 would be useful for other cell types and, in particular, for primary cells.

5. Most clinical and commercial applications of cryopreserved cells or tissues require a threshold level of post thaw viability, e.g., 50% post thaw viability. Low levels of post thaw viability diminish the effectiveness of the therapy and may potentially result in loss of life. For example, poor post thaw recovery of hematopoietic cells reduces the hematological recovery of patients undergoing bone marrow transplant and increases the risk of death from infection or other causes. WO 97/35472 fails to describe the post thaw viability of clinically relevant cells achieved using an arabinogalactan containing solution.

6. Therefore, WO 97/35472 provides no reasonable expectation that any particular arabinogalactan containing solution would be useful to cryopreserve cells employed in cellular-based therapies, e.g., freshly isolated lymphocytes, hematopoietic stem cells or ex vivo modified lymphocytes. Moreover, WO 97/35472 provides no reasonable expectation that the use of such a solution would result in a threshold level of post thaw viability for cells employed in cellular-based therapies.

7. In contrast, the present application represents a significant and needed contribution to the cryopreservation of therapeutically relevant cells including hematopoetic cells. In particular, the application describes a cryopreservation solution and method which results in high post thaw viability for an important cell type for both clinical and in vitro applications (e.g., lymphocytes), and a cryopreservation solution which is safe for human infusion.

8. I further declare that all statements made herein of my own knowledge are true, and that all statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 10/29/02

By: John C. Bischof, Ph.D.